Efficient ferrocifen anticancer drug and Bcl-2 gene therapy using lipid nanocapsules on human melanoma xenograft in mouse

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Mots-clés	gene therapy [13], Metal-based drug [14], nanoparticles [15], Passive targeting [16], SK-Mel28 [17]
Résumé en anglais	Metastatic melanoma has been described as a highly aggressive cancer with low sensibility to chemotherapeutic agents. New types of drug, such as metal-based drugs (ferrocifens) have emerged and could represent an alternative for melanoma treatment since they show interesting anticancer potential. Furthermore, molecular analysis has evidenced the role of apoptosis in the low sensibility of melanomas and especially of the key regulator, Bcl-2. The objective of this study was to combine two strategies in the same lipid nanocapsules (LNCs): i) gene therapy to modulate anti-apoptotic proteins by the use of Bcl-2 siRNA, and ii) ferrocifens as a new type of anticancer agent. The efficient gene silencing with LNCs was verified by the specific extinction of Bcl-2 in melanoma cells. The cellular toxicity of ferrocifens (ferrociphenol (FcDiOH) or Ansa-FcDiOH) was demonstrated, showing higher efficacy than dacarbazine. Interestingly, the association of siBcl-2 LNCs with Ansa-FcDiOH demonstrated a significant effect on melanoma cell viability. Moreover, the co-encapsulation of siRNA and ferrocifens was successfully performed into LNCs for animal experiments. A reduction of tumor volume and mass was proved after siBcl-2 LNC treatment and Ansa-FcDiOH LNC treatment, individually (around 25%). Finally, the association of both components into the same LNCs increased the reduction of tumor volume to about 50% compared to the control group. In conclusion, LNCs appeared to provide a promising tool for the co-encapsulation of a metal-based drug and siRNA.
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